

## **REMARKS**

### **I. Preliminary Remarks Regarding Amendments**

The Applicants do not intend by any amendments to abandon the subject matter of any claim previously presented. The Applicants reserve the right to pursue the subject matter of such claims during prosecution of this or subsequent applications. Furthermore, cancellation of 32-33 is not intended to change the scope or interpretation of the remaining pending claims.

Claims 7-24 and 31-33 stand rejected and are currently being examined. Claims 7, 8, 14, and 20 are amended herein. Claims 32-33 are canceled herein. Thus, claims 7-24 and 31 are currently pending.

In the Office Action, the rejection of claims 32-33 under 35 U.S.C. § 112, first paragraph, for assertedly lacking enablement commensurate with the scope of the claims was maintained. The rejection of claims 7-24 and 31-33 under 35 U.S.C. § 112, first paragraph, was also maintained for assertedly lacking written descriptive support commensurate with the scope of the claims. Claims 8-24, and 31-33 remain rejected under 35 U.S.C. § 112, second paragraph, for asserted indefiniteness for two reasons: 1) for reciting the phrase “a gene” that evidences decreased expression, in light of the claims assertedly still reciting the terms homolog and expression and activity of the homolog gene product which have not been defined, and 2) in light of the mutation in the homolog gene and gene product, which results in decreased expression, as not being clearly set forth in the claims. Reconsideration and withdrawal of the rejections is solicited for the reasons set out below. This response is timely filed as it is accompanied by a petition for an extension of time and the requisite fee.

### **II. Amendments**

Claim 12 is amended to remove a typographical error. Support for the amendment to claims 7, 8, 14, and 20 can be found at least at page 5 and at page 6. The amendment includes no new matter.

### **III. Patentability Arguments**

#### **A. The Scope of Enablement Rejection of Claims 32-33 under 35 U.S.C. § 112, First Paragraph, May Properly Be Withdrawn.**

Claims 32-33 stand rejected for reciting subject matter assertedly not described in the specification in a manner sufficient to enable any person skilled in the art to make and use the invention commensurate in scope with the claims. The Examiner holds that the specification does not reasonably provide enablement for the formulation of the claimed genus compositions into vaccines. Applicants respectfully disagree, one of skill in the art could make and use the compositions of claims 31-33 without undue experimentation.

Example 3 demonstrates that an attenuated *Pasteurellaceae* bacteria comprising a mutation resulting in decreased atpG activity provides protective immunity (see page 37, Table 1). Example 11 demonstrates that such bacteria are safe and effective. The art cited in the rejection does not contradict the express teachings of the specification. The Humbert *et al.* reference does not indicate or suggest that an attenuated *Pasteurellaceae* bacteria comprising a mutation resulting in decreased atpG activity would not provide protective immunity. Furthermore, although there may be increased risks with using an attenuated bacteria strain that is resistant to certain antibiotics, such bacteria still can be capable of being immunogenic and providing protective immunity. This risk-benefit analysis is rightfully in the realm of the Federal Drug Administration not the Patent and Trademark Office.

Nonetheless, in an effort to expedite prosecution of the application, claims 32-33 are canceled herein. Applicants respectfully request withdrawal of the rejection.

#### **B. The Written Description Rejection of Claims 7-24 and 31-33 under 35 U.S.C. §112, First Paragraph, May Properly Be Withdrawn.**

The rejection of claims 7-24 and 31-33 under 35 U.S.C. §112, first paragraph, is maintained for assertedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the invention. The Office Action at page 6 asserts that no specific genes (open reading frames) that encode species homologues of the identified nucleic acid sequences meet the written description requirement by providing a representative number of species of the claimed genus of recombinant bacteria

with mutations in species homologues of nucleic acid sequences of SEQ ID NO: 3 and are mutated to evidence reduced expression of the encoded gene product. The Applicants respectfully disagree.

First, paragraph 18 states that it is the position of the examiner that the patentable novelty of the instant Application is directed to mutations in a polynucleotide sequence that encodes for the gamma subunit of ATPase of two species of *Pasteurellaceae*. Applicants respectfully assert this position of patentability is too narrow. Applicant should be permitted to claim as broadly as the art allows and the specification describes and enables. Applicants have demonstrated that *Pasteurellaceae* bacteria having decreased atpG biological activity are attenuated and are capable of providing protective immunity against wild-type bacteria of the same strain. The art of record in this application does not disclose *Pasteurellaceae* bacteria having decreased atpG biological activity. Furthermore, using the specification as a guide, one of ordinary skill in the art could make and use the invention of the pending claims without undue experimentation. Therefore, there is no reason to limit the claims to the exemplary embodiments in the specification.

The claims are not directed to novel nucleic acids, which arguably would require a more detailed description of their structure. Nor is the claimed invention directed to "mutations" as alleged in paragraph 18 of the Office Action. Whether the sequence of the atpG homolog of a *Pasteurellaceae* bacteria is known in the art or not is not material. The claims are directed, e.g., to an attenuated bacteria comprising an atpG mutation. As demonstrated by the Examples, it is not necessary to know the sequence of a atpG homolog to make and use the claimed invention. It was not necessary to know the sequence of the *P. multocida* atpG gene to construct the mutant in Example 1 or to demonstrate the mutant is attenuated in Example 2. This is true of other *Pasteurellaceae* family members as demonstrated in Example 5 and there is nothing of record to suggest that this would not be true for any *Pasteurellaceae* family members. Therefore, because prior knowledge of the sequence of any species homolog is not necessary to practice the claimed invention, the claims should not be held to the standard of nucleic acid claims. The examiner has failed to provide reasoning or evidence to support the rejection, except to cite older, DNA invention cases (*Amgen*, *Fiers*) which are distinguishable on their facts. Applicant respectfully requests reconsideration of the rejection.

**C. The Indefiniteness Rejections of Claims 8-24 and 31-33 under 35 U.S.C. §112, Second Paragraph, May Properly Be Withdrawn.**

1. The Examiner maintains the rejection of claims 8-24 and 31-33 under 35 U.S.C. §112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner rejected claims 8-24 and 31-33 and asserted that the amendment of the claims to recite "a mutation in the atpG protein coding region of SEQ ID NO: 3" and the amendment to claim 7 to recite "resulting in decreased atpG biological activity" partially obviates the rejection, but does not fully clarify what is meant by "species homolog" and what the species homolog "gene product" is. The Applicants respectfully disagree.

Page 5 of the specification states, as understood in the art, "species homologs include genes found in two or more different species which possess substantial polynucleotide sequence homology and possess the same, or similar, biological function and/or properties." As understood by those in the art, sharing a conserved sequence is not sufficient to consider two genes homologs. New species homologs of known genes are described in the art all the time. Finding and/or detecting atpG species homologs is described in the Examples. Thus, given the direction provided by the specification and the understanding of those of skill in the art, the term "species homolog" does not render the claims indefinite.

2. The Examiner maintains the rejection of claims 7-24 and 31-33 under 35 U.S.C. §112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner rejected claims 7-24 and 31-33 because the location in the gene where the mutation that will decrease gene product expression is not distinctly claimed. The Applicants respectfully disagree.

The Applicants submit that they do not need to specifically point out where the mutation is located in the sequence. Indeed, in claims to transgenic animals comprising a "knockout" of a particular endogenous gene, the claims are **not** limited to the specific disruption or SEQ ID NO. disclosed, see *e.g.*, 5,714,667; 5,777,195; 6,087,555; and 6,100,445. The presently claimed attenuated bacteria are analogous to knockout animals having a particular phenotype. The rejection does not put forth any reasoning as to why, for purposes of definiteness, a claim directed to a bacteria lacking expression of a particular gene

must distinctly claim the mutation, whereas a claim directed to an animal lacking expression of a particular gene does not.

Furthermore, amendment to claims 8, 14, and 20 obviates any perceived ambivalence as to the cause of decreased atpG biological activity by reciting that the mutation is in the coding region of the atpG and, in some embodiments, biological activity is decreased due to decreased atpG gene product expression.

3. The Examiner maintains the rejection of claims 8, 14, and 20 under 35 U.S.C. §112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner rejected claims 8, 14, and 20 because the claim language recited assertedly does not show clear delineation as to what type of mutation is being introduced into the claimed bacterium. The Applicants respectfully disagree.

However, in order to expedite prosecution of the application, the Applicants have amended the claims to remove the clause “of an atpG gene product encoded by the mutated atpG protein coding region.” Thus, in view of amendments to the claims, the objection is now rendered moot and should be withdrawn.

4. The Examiner rejected claims 8-12, 14-18, and 21-24 under 35 U.S.C. §112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner rejected claims 8-12, 14-18, and 21-24 because claim they depend ultimately from claim 7 which lacks antecedent basis for the phrase “atpG gene.” The Applicants have amended claim 7 to add the phrase “atpG gene”. Thus, in view of amendment, the objection is now rendered moot and should be withdrawn.

The Examiner also rejected claim 8 because it assertedly broadens the scope of claim 7 from which it depends by defining the mutation to be “decreased gene expression.” The Applicants respectfully disagree. Decreased gene expression can occur from a mutation in the protein coding region as defined in claim 7. The Applicants submit that the use of the phrase “decreased gene expression” does not broaden the scope of claim 8. Furthermore, the Applicants submit that they need not define the specific mutation which causes the decreased gene expression, nor need they define the specific mutation that results in decreased gene expression in the homolog. Nevertheless, claim 8 is amended herein to clarify that the

mutation in the protein coding region of atpG results in decreased expression of the atpG gene product. The rejection should be withdrawn.

#### IV. CONCLUSION

In view of the amendments and remarks made herein, Applicants respectfully submit that claims 7-24 are in condition for allowance and respectfully request expedited notification of same. Should the Examiner have any questions of form or substance, she is welcomed to contact the undersigned at the telephone number below.

Respectfully submitted,

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